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Resolving the spatiotemporal map of the tight junction interactome

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Epithelial cell polarization is a fundamental organizing principle during early embryonic development, and later differentiation into specific tissues and organs. It is known that epithelial transition involves asymmetry, where cells polarize into apical, lateral, and basal plasma membrane domains. However, how the identity of the polarized membrane is established and communicated to the transcription machinery within the nucleus? Answering these fundamental questions in biology requires development of new tools that will allow us to systematically map the molecular interactions at the cell-cell junctions (tight junctions) during the establishment of epithelial polarity.To overcome this, I am developing a novel proteomic based chemical tool to spatiotemporally map the protein and lipid interaction networks of polarized cell membrane domains in living cells. Combining the state-of-art biorthogonal click chemistry with APEX2 we can identify and purify with high specificity the interactome of the proteins genetically tagged with the tool. This approach provides us with a quantitative picture of where and when adhesion, polarity, and transcription proteins interact during the tissue formation process. Together with quantitative and super-resolution microscopy of three-dimensional cell culture, will allow us to develop a mechanistic understanding of how the polarization network stablishes and how it feeds back to cell fate.

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